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|---|---|---|
| On page 15 | line 19 | delete "a" (at the end of the line) |
| On page 17 | line 9 | change "lower collision free" to --lower, collision free,-- |
| | line 13 | change "continuos" to --continuous-- |
| On page 21 | line 21 | delete "hexapole" |
| On page 22 | line 6 | delete "the" |
| On page 23 | line 23 | change "enter" to --entering TOF pulsing region 30-- |

In the Claims:

Please cancel Claims 1-32 and add new claims 33-154 as follows:

33. An apparatus for analyzing chemical species comprising:
(a) at least one vacuum pumping stage;
(b) an ion source for producing ions from a sample substance;
(c) a multipole ion guide located in at least one of said vacuum pumping stages;
(d) a Time-Of-Flight mass analyzer;
(e) means for delivering ions from said ion source into said multipole ion guide,
(f) means for delivering ions from said multipole ion guide into said Time-Of-Flight mass analyzer;
(g) means for fragmenting ions located in said multipole ion guide comprising means for application of electrical voltages to said multipole ion guide to operate said multipole ion guide in a manner which results in fragmentation of ions located in said multipole ion guide; and
(h) means for conducting Time-Of-Flight mass analysis of ions from said multipole ion guide.

34. An apparatus according to Claim 33, wherein said ion source produces ions at substantially atmospheric pressure.

35. An apparatus according to Claim 33, wherein said ion source is an Electrospray ion source.

36. An apparatus according to Claim 33, wherein said ion source is an Atmospheric Pressure Chemical Ionization Source.

37. An apparatus according to Claim 33, wherein said ion source is an Inductively Coupled Plasma ion source.

38. An apparatus according to Claim 33, wherein said ion source is a glow discharge ion source.

39. An apparatus according to Claim 33, wherein said apparatus comprises a Time-Of-Flight tube axis, and wherein ions are delivered from said multipole ion guide to said

Time-Of-Flight mass analyzer in a direction substantially in line with said Time-Of-Flight tube axis.

40. An apparatus according to Claim 33, wherein said Time-Of-Flight mass analyzer includes an ion reflector.

41. An apparatus according to Claim 33, wherein said multipole ion guide is a quadrupole.

42. An apparatus according to Claim 33, wherein said multipole ion guide is a hexapole.

43. An apparatus according to Claim 33, wherein said multipole ion guide is an octopole.

44. An apparatus according to Claim 33, wherein said multipole ion guide is configured with a number of poles greater than eight.

45. An apparatus according to Claim 33, wherein said means for fragmenting ions located in said multipole ion guide further comprises means for controlling the electrical voltages applied to said multipole ion guide.

46. An apparatus according to Claim 33, wherein said multipole ion guide has a configuration of electrical potentials applied to said multipole ion guide to cause fragmentation of ions in said multipole ion guide.

47. An apparatus according to Claim 33, wherein said means for fragmenting ions further comprises an exit lens and an entrance lens for said multipole ion guide.

48. An apparatus according to Claim 33, wherein said multipole ion guide comprises entrance and exit ends and wherein said means for fragmenting ions further comprises electrodes located at said entrance and exit ends of said multipole ion guide.

49. An apparatus according to Claim 47, comprising means for applying electrical voltages to said exit lens and said entrance lens.

50. An apparatus according to Claim 48, comprising means for applying electrical voltages to said electrodes.

51. An apparatus according to Claim 33, wherein said means for fragmenting ions comprises multipole ion guide entrance and exit electrode elements, means for controlling the electrical voltages applied to said multipole ion guide, means for applying electrical voltages applied to said multipole ion guide entrance and exit electrode elements, and means for controlling the electrical voltages applied to said multipole ion guide entrance and exit electrode elements.

52. An apparatus according to Claim 33, wherein ions are trapped in said multipole ion

guide.

53. An apparatus according to Claim 33, wherein ions are trapped in said multipole ion guide, some of the trapped ions being fragmented.

54. An apparatus according to Claim 45, wherein said means for controlling the electrical voltages applied to said multipole ion guide can be adjusted to cause fragmentation of selected m/z values of ions in said internal volume of said multipole ion guide by Collision Induced Dissociation of ions with neutral background molecules.

55. An apparatus according to Claim 54, wherein said Collisional Induced Dissociation of selected m/z values of ions is caused by resonant frequency excitation.

56. An apparatus according to Claim 33, wherein selected m/z values of ions are trapped in said multipole ion guide and undergo Collisional Induced Dissociation.

57. An apparatus according to Claim 33, wherein a portion of said internal volume of said multipole ion guide has a pressure in the range of $10^{-4}$ to $10^{-2}$ torr.

58. An apparatus according to Claim 33, wherein a portion of said internal volume of said multipole ion guide has a pressure in the range of $10^{-4}$ to $10^{-1}$ torr.

59. An apparatus according to Claim 48, wherein said means for controlling said electrical voltages applied to said multipole ion guide and said means for controlling said electrical voltages applied to said electrode elements can be adjusted to select the range of m/z values of ions transmitted through said multipole ion guide.

60. An apparatus according to Claim 51, wherein said means for controlling said electrical voltages applied to said multipole ion guide and said means for controlling said electrical voltages applied to said electrode elements can be adjusted during the data acquisition period such that a portion of ions produced by said ion source continuously enter said multipole ion guide.

61. An apparatus according to Claim 51, wherein said means for controlling said electrical voltages applied to said multipole ion guide and said means for controlling said electrical voltages applied to said electrode elements can be adjusted during the data acquisition period such that a portion of ions produced by said ion source are prevented from continuously entering said multipole ion guide.

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62. An apparatus for analyzing chemical species comprising:
(a) at least one vacuum pumping stage;
(b) an ion source for producing ions from a sample substance;
(c) a multipole ion guide located in at least one of said vacuum pumping stages;
(d) a Time-Of-Flight mass analyzer;

(e) means for delivering ions from said ion source into said multipole ion guide;
(f) means for delivering ions from said multipole ion guide into said Time-Of-Flight mass analyzer;
(g) means for conducting mass to charge selection of ions located in said multipole ion guide comprising means for applying electrical voltages to said multipole ion guide to operate said multipole ion guide in a manner which results in mass to charge selection of ions located in said multipole ion guide; and
(h) means for conducting Time-Of-Flight mass analysis of ions from said multipole ion guide.

38 ~~63~~. An apparatus according to Claim 37 ~~62~~, wherein said ion source produces ions at substantially atmospheric pressure.

39 ~~64~~. An apparatus according to Claim 37 ~~62~~, wherein said ion source is an Electrospray ion source.

40 ~~65~~. An apparatus according to Claim 37 ~~62~~, wherein said ion source is an Atmospheric Pressure Chemical Ionization Source.

41 ~~66~~. An apparatus according to Claim 37 ~~62~~, wherein said ion source is an Inductively Coupled Plasma ion source.

42 ~~67~~. An apparatus according to Claim 37 ~~62~~, wherein said ion source is a glow discharge ion source.

43 ~~68~~. An apparatus according to Claim 37 ~~62~~, wherein said apparatus comprises a Time-Of-Flight tube axis, and wherein ions are delivered from said multipole ion guide to said Time-Of-Flight mass analyzer in a direction substantially in line with said Time-Of-Flight tube axis.

44 ~~69~~. An apparatus according to Claim 37 ~~62~~, wherein said Time-Of-Flight mass analyzer includes an ion reflector.

45 ~~70~~. An apparatus according to Claim 37 ~~62~~, wherein said multipole ion guide is a quadrupole.

46 ~~71~~. An apparatus according to Claim 37 ~~62~~, wherein said multipole ion guide is a hexapole.

47 ~~72~~. An apparatus according to Claim 37 ~~62~~, wherein said multipole ion guide is an octopole.

48 ~~73~~. An apparatus according to Claim 37 ~~62~~, wherein said multipole ion guide is configured with a number of poles greater than eight.

49 ~~74~~. An apparatus according to Claim 37 ~~62~~, wherein said means for conducting mass selection of ions located in said multipole ion guide further comprises means for

controlling the electrical voltages applied to said multipole ion guide.

75. An apparatus according to Claim 62, wherein said multipole ion guide has a configuration of electrical potentials applied to said multipole ion guide to cause mass to charge selection of ions located in said multipole ion guide.

76. An apparatus according to Claim 62, wherein said means for conducting mass selection of ions further comprises an exit lens and an entrance lens for said multipole ion guide.

77. An apparatus according to Claim 74, wherein said multipole ion guide comprises entrance and exit ends and wherein said means for conducting mass selection of ions comprises electrodes located at said entrance and exit ends of said multipole ion guide.

78. An apparatus according to Claim 76, comprising means for applying electrical voltages to said exit lens and said entrance lens.

79. An apparatus according to Claim 77, comprising means for applying electrical voltages to said electrodes.

80. An apparatus according to Claim 62, wherein said means for conducting mass selection of ions comprises multipole ion guide entrance and exit electrode elements, means for controlling the electrical voltages applied said multipole ion guide, means for applying electrical voltages applied to said multipole ion guide entrance and exit electrode elements, and means for controlling the electrical voltages applied to said multipole ion guide entrance and exit electrode elements.

81. An apparatus according to Claim 62, wherein ions are trapped in said multipole ion guide.

82. An apparatus according to Claim 62, wherein selected m/z values of the ions are trapped in said multipole ion guide.

83. An apparatus according to Claim 62, wherein selected m/z values of ions are trapped in said multipole ion guide and undergo Collisional Induced Dissociation.

84. An apparatus according to Claim 62, wherein a portion of said internal volume of said multipole ion guide has a pressure in the range of $10^{-4}$ to $10^{-2}$ torr.

85. An apparatus according to Claim 62, wherein a portion of said internal volume of said multipole ion guide has a pressure in the range of $10^{-4}$ to $10^{-1}$ torr.

86. An apparatus according to Claim 77, wherein said means for controlling said electrical voltages applied to said poles of said multipole ion guide and said means for

controlling said electrical voltages applied to said electrode elements can be adjusted to select the range of m/z values of ions transmitted through said multipole ion guide.

87. An apparatus according to Claim 77, wherein said means for controlling said electrical voltages applied to said poles of said one multipole ion guide and said means for controlling said electrical voltages applied to said electrode elements can be adjusted to select the range of m/z values of ions trapped in said multipole ion guide.

88. An apparatus according to Claim 80, wherein said means for controlling said electrical voltages applied to said multipole ion guide and said means for controlling said electrical voltages applied to said electrode elements can be adjusted during the data acquisition period such that a portion of ions produced by said ion source continuously enter said multipole ion guide.

89. An apparatus according to Claim 80, wherein said means for controlling said electrical voltages applied to said multipole ion guide and said means for controlling said electrical voltages applied to said electrode elements can be adjusted during the data acquisition period such that a portion of ions produced by said ion source are prevented from continuously entering said multipole ion guide.

90. An apparatus for analyzing chemical species comprising:
(a) at least one vacuum pumping stage;
(b) an ion source for producing ions from a sample substance;
(c) a multipole ion guide located in at least one of said vacuum pumping stages;
(d) a Time-Of-Flight mass analyzer;
(e) means for delivering ions from said ion source into at least one of said multipole ion guides,
(f) means for delivering ions from at least one of said multipole ion guides into said Time-Of-Flight mass analyzer;
(g) means for fragmenting ions located in at least one of said multipole ion guides comprising means for application of electrical voltages to at least one of said multipole ion guides to operate at least one of said multipole ion guides in a manner which results in fragmentation of ions located in at least one of said multipole ion guides;
(h) means for conducting mass to charge selection of ions located in at least one of said multipole ion guides comprising means for applying electrical voltages to at least one of said multipole ion guides to operate at least one of said multipole ion guide in a manner which results in mass to charge selection of ions located in at least one of said multipole ion guides; and
(i) means for conducting Time-Of-Flight mass analysis of ions from said at least one of said multipole ion guides.

91. An apparatus according to Claim 90, wherein said ion source produces ions at

substantially atmospheric pressure.

92. An apparatus according to Claim 90, wherein said ion source is an Electrospray ion source.

93. An apparatus according to Claim 90, wherein said ion source is an Atmospheric Pressure Chemical Ionization Source.

94. An apparatus according to Claim 90, wherein said ion source is an Inductively Coupled Plasma ion source.

95. An apparatus according to Claim 90, wherein said ion source is a glow discharge ion source.

96. An apparatus according to Claim 90, wherein said apparatus comprises a Time-Of-Flight tube axis, and wherein ions are delivered from at least one of said multipole ion guides to said Time-Of-Flight mass analyzer in a direction substantially in line with said Time-Of-Flight tube axis.

97. An apparatus according to Claim 90, wherein said Time-Of-Flight mass analyzer includes an ion reflector.

98. An apparatus according to Claim 90, wherein at least one of said multipole ion guides is a quadrupole.

99. An apparatus according to Claim 90, wherein at least one of said multipole ion guides is a hexapole.

100. An apparatus according to Claim 90, wherein at least one of said multipole ion guides is an octopole.

101. An apparatus according to Claim 90, wherein at least one of said multipole ion guides is configured with a number of poles greater than eight.

102. An apparatus according to Claim 90, wherein said means for conducting mass selection of ions located in at least one of said multipole ion guides and said means for fragmenting ions located in at least one of said multipole ion guides each comprise means for controlling the electrical voltages applied to at least one of said multipole ion guides.

103. An apparatus according to Claim 90, wherein at least one of said multipole ion guides has a configuration of electrical potentials applied thereto to cause fragmentation of ions located in at least one of said multipole ion guides and mass to charge selection of ions located in at least one of said multipole ion guides.

104. A method of analyzing chemical species utilizing an ion source, a vacuum system with at least one vacuum pumping stage, a multipole ion guide located in at least one of said vacuum pumping stages, and a Time-Of-Flight mass analyzer, said method comprising:

(a) producing ions from a sample substance using said ion source;

(b) directing said ions into said multipole ion guide;

(c) fragmenting ions in said multipole ion guide to form an ion population in said multipole ion guide which contains fragment ions; and,

(d) conducting mass to charge analysis of said ion population with said Time-Of-Flight mass analyzer.

105. A method according to Claim 104, wherein said ions are produced using Electrospray ionization.

106. A method according to Claim 104, wherein said ions are produced using Atmospheric Pressure Chemical Ionization.

107. A method according to Claim 104, wherein said ions are produced using Inductively Coupled Plasma Ionization.

108. A method according to Claim 104, wherein said ions are produced using glow discharge ionization.

109. A method according to Claim 104, wherein ions are directed into said multipole ion guide from said ion source while ion fragmentation is occurring in said multipole ion guide.

110. A method according to Claim 104, wherein ions are prevented from entering said multipole ion guide from said ion source while ion fragmentation is occurring in said multipole ion guide.

111. A method according to Claim 104, wherein m/z value ions are selected in said multipole ion guide using resonant frequency ejection of unwanted ions.

112. A method according to Claim 104, wherein m/z value ions are selected in said multipole ion guide by applying selected RF amplitude potentials to said multipole ion guide to eject unwanted ions from said multipole ion guide.

113. A method according to Claim 104, wherein m/z value ions are selected in said multipole ion guide ions by applying selected RF and DC amplitude potentials to said multipole ion guide to ejected unwanted ions from said multipole ion guide.

114. A method according to Claim 104, wherein ions are fragmented in said multipole ion

guide by resonant frequency excitation collisional induced dissociation.

115. A method according to Claim 104, wherein ions are fragmented in said multipole ion guide by releasing ions from the exit end of said multipole ion guide, raising the potential of said released ions, accelerating said ions with raised potential in the reverse direction back into said exit end of said multipole ion guide and colliding said reverse direction accelerated ions with neutral background gas present in said multipole ion guide to cause collisional induced dissociation of said ions.

116. A method according to Claim 104, wherein said multipole ion guide is operated in ion trapping mode.

117. A method according to Claim 104, wherein said ions are pulsed from said multipole ion guide into a Time-Of-Flight mass analyzer flight tube.

118. A method according to Claim 104, wherein ions released from said multipole ion guide are pulsed into a Time-Of-Flight tube drift region.

119. A method according to Claim 116, wherein ions are trapped in said multipole ion guide, and ions are pulsed into said Time-Of-Flight mass analyzer such that only a portion of said ions trapped in said multipole ion guide is released for each pulse of ions into said Time-Of-Flight mass analyzer.

120. A method of analyzing chemical species utilizing an ion source, a vacuum system with at least one vacuum pumping stage, a multipole ion guide located in at least one of said vacuum pumping stages, and a Time-Of-Flight mass analyzer, said method comprising:

(a) producing ions from a sample substance using said ion source;
(b) directing the ions into said multipole ion guide;
(c) conducting ion mass to charge selection in said multipole ion guide to produce an ion population of mass to charge selected ions; and,
(d) conducting mass to charge analysis of said selected ions with said Time-Of-Flight mass analyzer.

121. A method according to Claim 120, wherein said ions are produced using Electrospray ionization.

122. A method according to Claim 120, wherein said ions are produced using Atmospheric Pressure Chemical Ionization.

123. A method according to Claim 120, wherein said ions are produced using Inductively Coupled Plasma Ionization.

109 ~~124~~. A method according to Claim 105, wherein said ions are produced using glow discharge ionization.

110 ~~125~~. A method according to Claim 105, wherein said ion mass to charge selection is conducted in said multipole ion guide by ejecting ions with unwanted mass to charge values from said multipole ion guide.

111 ~~126~~. A method according to Claim 105, wherein ions are directed into said multipole ion guide from said ion source while ion mass to charge selection is occurring in said multipole ion guide.

112 ~~127~~. A method according to Claim 105, wherein ions are prevented from entering said multipole ion guide from said ion source while ion mass to charge selection is occurring in said multipole ion guide.

113 ~~128~~. A method according to Claim 105, wherein unwanted ions are ejected from said multipole ion guide during said ion mass to charge selection using resonant frequency ejection.

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114 ~~129~~. A method according to Claim 105, wherein unwanted ions are ejected from said multipole ion guide during said ion mass to charge selection by applying selected RF amplitude potentials to said multipole ion guide.

115 ~~130~~. A method according to Claim 105, wherein unwanted ions are ejected from said multipole ion guide during said ion mass to charge selection by applying selected RF and DC amplitude potentials to said multipole ion guide.

116 ~~131~~. A method according to Claim 105, wherein said ions are pulsed from said multipole ion guide into a Time-Of-Flight mass analyzer flight tube.

117 ~~132~~. A method according to Claim 105, wherein ions released from said multipole ion guide are pulsed into a Time-Of-Flight tube drift region.

118 ~~133~~. A method according to Claim 105, wherein said multipole ion guide is operated in ion trapping mode.

119 ~~134~~. A method according to Claim 118, wherein ions are trapped in said multipole ion guide, and ions are pulsed into said Time-Of-Flight mass analyzer such that only a portion of said ions trapped in said multipole ion guide is released for each pulse of ions into said Time-Of-Flight mass analyzer.



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135. A method of analyzing chemical species utilizing an ion source, a vacuum system with at least one vacuum pumping stage, at least one multipole ion guide, each of said multipole ion guides being located in at least one of said vacuum pumping stages, and a Time-Of-Flight mass analyzer, said method comprising:

(a) producing ions from a sample substance using said ion source;

(b) directing the ions into at least one of said multipole ion guides;

(c) conducting ion mass to charge selection in at least one of said multipole ion guides;

(d) fragmenting said selected mass to charge value ions in at least one of said multipole ion guides to form fragment ions in at least one of said multipole ion guides; and,

(e) conducting mass to charge analysis of said fragment ions with said Time-Of-Flight mass analyzer.

136. A method according to Claim 135, wherein said ions are produced using Electrospray ionization.

137. A method according to Claim 135, wherein said ions are produced using Atmospheric Pressure Chemical Ionization.

138. A method according to Claim 135, wherein said ions are produced using Inductively Coupled Plasma Ionization.

139. A method according to Claim 135, wherein said ions are produced using glow discharge ionization.

140. A method according to Claim 135, wherein said ion mass to charge selection and said fragmenting of said selected mass to charge value ions are both conducted in the same one of said multipole ion guides.

141. A method according to Claim 135, wherein said ion mass to charge selection and said fragmenting of said selected mass to charge value ions are not both conducted in the same one of said multipole ion guides.

142. A method according to Claim 135, wherein ions are directed into at least one of said multipole ion guides from said ion source while ion mass to charge selection is occurring in at least one of said multipole ion guides.

143. A method according to Claim 135, wherein ions are directed into at least one of said multipole ion guides from said ion source while ion fragmentation is occurring in at least one of said multipole ion guides.

144. A method according to Claim 135, wherein ions are directed into at least one of said multipole ion guides from said ion source while ion mass to charge selection and ion

fragmentation is occurring in at least one of said multipole ion guides.

130 ~~145~~. A method according to Claim ~~135~~ 120, wherein ions are prevented from entering at least one of said multipole ion guides from said ion source while ion fragmentation is occurring in at least one of said multipole ion guides.

131 ~~146~~. A method according to Claim ~~135~~ 120, wherein ions are prevented from entering at least one of said multipole ion guides from said ion source while ion mass to charge selection is occurring in at least one of said multipole ion guides.

132 ~~147~~. A method according to Claim ~~135~~ 120, wherein unwanted ions are ejected from said multipole ion guide during said ion mass to charge selection using resonant frequency ejection.

133 ~~148~~. A method according to Claim ~~135~~ 120, wherein unwanted ions are ejected from said multipole ion guide during said ion mass to charge selection by applying selected RF amplitude potentials to said multipole ion guide.

Cancel A1 134 ~~149~~. A method according to Claim ~~135~~ 120, wherein unwanted ions are ejected from said multipole ion guide during said ion mass to charge selection by applying selected RF and DC amplitude potentials to said multipole ion guide.

135 ~~150~~. A method according to Claim ~~135~~ 120, wherein ions are fragmented in at least one of said multipole ion guides by resonant frequency excitation collisional induced dissociation.

136 ~~151~~. A method according to Claim ~~135~~ 120, wherein ions are fragmented in at least one of said multipole ion guides by releasing ions from the exit end of at least one of said multipole ion guides, raising the potential of said released ions, accelerating said ions with raised potential in the reverse direction back into said exit end of at least one of said multipole ion guides and colliding said reverse direction accelerated ions with neutral background gas present in at least one of said multipole ion guides to cause collisional induced dissociation of said ions.

137 ~~152~~. A method according to Claim ~~135~~ 120, wherein at least one of said multipole ion guides is operated in ion trapping mode, and wherein ions are directed into at least one of said multipole ion guides operated in ion trapping mode and wherein said fragmenting of said ions is conducted with ions trapped in at least one of said multipole ion guides.

139 ~~153~~. A method according to Claim ~~135~~ 120, wherein said ions are pulsed from at least one of said said multipole ion guides into a Time-Of-Flight mass analyzer flight tube.

140 ~~154~~. A method according to Claim ~~135~~ 120, wherein ions are released from at least one of said multipole ion guides and are pulsed into a Time-Of-Flight tube drift region.



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155. A method according to Claim 152, wherein ions are trapped in at least one of said multipole ion guide, and ions are pulsed into said Time-Of-Flight mass analyzer such that only a portion of said ions trapped in said multipole ion guide is released for each pulse of ions into said Time-Of-Flight mass analyzer.

156. A method according to Claim 135, wherein at least one of said multipole ion guides is operated in ion trapping mode, and wherein ions are directed into at least one of said multipole ion guides operated in ion trapping mode and wherein said ion mass to charge selection is conducted with ions trapped in at least one of said multipole ion guides.

**Remarks**

Receipt is acknowledged of the final Office Action of April 21, 1998. In response thereto, Applicant is filing the present CPA application, including the present Preliminary Amendment and Remarks. Reconsideration of the application and a three month extension of the time provided for response to the final Office Action are respectfully requested. A check in payment of the necessary fees for the CPA application, for the extension, and for the new claims is enclosed. Should any additional fees or extensions be necessary, payment of the appropriate amount and/or granting of the appropriate extension is so requested, and the Commissioner is directed to debit our deposit account, Account No. 02-2105 for the amounts required.

In response to the Office Action, the application has been amended by deleting the prior claims and adding new Claims 33-154, to more distinctly and particularly point out the subject matter which Applicant considers to be the invention and to claim the invention in the scope to which Applicant is believed to be entitled. All of the new claims are believed to be patentable over the cited references, for the reasons set forth below.